EXHIBIT D

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/301,820	04/15/2021	Grahame Woollam	P-257-US9/71TD-343862-US9	1236

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EXAMINER
PIHONAK, SARAH

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
02/10/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 17/301,820	Applicant(s) Woollam, Grahame	
	Examiner SARAH PIHONAK	Art Unit 1627	AIA (FITF) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 11/22/22.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL.** 2b) ☑ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 41-43,48-50,53 and 55-68 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 41-43,48-50,53 and 55-68 is/are rejected.

8) ☐ Claim(s) _____ is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☑ The drawing(s) filed on 4/15/21 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Priority

This application, filed on 4/15/21, is a CON of 16715225, filed on 12/16/19. 16715225 is a CON of 16130079, filed 09/13/2018. 16130079 is a CON of 15677264, filed 08/15/2017.

15677264 is a CON of 15206877, filed 07/11/2016.

15206877 is a CON of 14955515, filed 12/01/2015.

14955515 is a CON of 14547455, filed 11/19/2014.

14547455 is a CON of 13973174, filed 08/22/2013.

13973174 is a DIV of 12835964, filed 07/14/2010.

12835964 claims priority from provisional application 61225803, filed 07/15/2009. The effective filing and priority date of the claims is 7/15/2009.

Status of Claims

1. Claims 41-43, 48-50, 53, 55-68 are pending as of 11/22/22. Claims 1-40, 44-47, 51-52, and 54 have been canceled.

2. Claims 41-43, 48-50, 53, 55-68 were examined and are rejected.

Claim Rejection-Statutory Double Patenting

3. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and

useful process... may obtain a patent therefor..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the claims that are directed to the same invention so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 62-64 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 32, 34, and 36 of copending Application No. 17841567 (reference application).

Copending claims 32, 34, and 36 are shown below with the corresponding claims 62-64 of the instant application.

32. (Previously Presented) A pharmaceutical composition comprising: a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester that is dissolved in a solvent; wherein the crystalline freebase is characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1.

62. (New) A pharmaceutical composition comprising: a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in a solution; wherein the crystalline freebase is characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1.

These claims are identical in scope, as both sets of claims are drawn to a pharmaceutical composition comprising the same crystalline form of the same compound in solution, i.e., dissolved in a solvent.

34. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, and further characterized by having five or more additional diffraction peaks at 2θ values selected from 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1, wherein the crystalline freebase is dissolved in the pharmaceutically acceptable carrier.

63. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, and further characterized by having five or more additional diffraction peaks at 2θ values selected from 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1, wherein the crystalline freebase is in solution with the pharmaceutically acceptable carrier.

These claims are identical in scope, as both sets of claims are drawn to a pharmaceutical composition comprising a pharmaceutically acceptable carrier and the same crystalline form of the same compound dissolved in a pharmaceutically acceptable carrier, i.e., in solution with a pharmaceutically acceptable carrier.

36. (Previously Presented) A pharmaceutical composition comprising a solution of a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by (i) a powder x-ray diffraction comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1 or (ii) a melting point of about 125° C, dissolved in a carrier.

64. (New) A pharmaceutical composition comprising a solution of a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by (i) a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1 or (ii) a melting point of about 125°C.

These claims are identical in scope, as both sets of claims are drawn to a pharmaceutical composition comprising a solution of the same crystalline form of the same compound, i.e., dissolved in a carrier.

This is a provisional statutory double patenting rejection since the claims directed to the same invention have not in fact been patented.

Claim Rejections-Nonstatutory Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 41-43, 48-50, 53, and 55-68 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-4, 8-10, and 16 of U.S. Patent No. 8541451 B2 in view of Axt et. al., WO 2006099165 A1, cited in an IDS. The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about 5. The claims of US '451 are drawn to a crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1; further characterized by having five or more additional diffraction peaks at 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1; designated as Form III; and having a melting point of about 125° C.; and a process of preparing this crystalline form. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1; and claim 49 of the instant application recites the crystalline form to have a melting point of about 125°C. Instant claims 42-43 recite the composition to comprise an aqueous pharmaceutical carrier; instant claim 48 recites the composition as isotonic; claim 55 recites the composition to be buffered with a citrate buffer; and instant claim 56 recites the amount of crystalline freebase compound in the composition to range from about 0.05 µg-10 mg/mL. Although the patented claims don't explicitly recite these

limitations, it would have been prima facie obvious to have incorporated an isotonic aqueous carrier, a citrate buffer, and the crystalline freebase compound in an amount from about 0.05 µg-10 mg/mL in view of Axt. Axt teaches crystalline forms of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in pharmaceutical compositions for treating pulmonary disorders (title & abstract; p. 2, lines 10-14 and 20-24). Axt teaches a specific embodiment wherein the composition comprises an isotonic aqueous solution containing the crystalline form of the compound, wherein the composition has a pH between 4-6, and is buffered with a citrate buffer (p. 3, lines 3-9). Axt further teaches an embodiment wherein the amount of the crystalline form of the compound present in the composition is from about 0.05 µg-10 mg/mL (p. 16, lines 25-30). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have incorporated these limitations into a pharmaceutical composition comprising a crystalline freebase of the patented compound. The instant and patented claims are not patentably distinct because both sets of claims are drawn to products comprising the same compound in the same crystalline form. The process of preparing the crystalline form recited in claim 16 of US '451 is not patentably distinct from the instant claims, since the process would have necessarily produced the compound of the instant claims.

5. Claims 41-43, 48-50, 53, and 55-68 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-4, 6-10, and 13-17 of U.S. Patent No. 9226896 B2 in view of Axt et. al., WO 2006099165 A1, cited in an IDS. The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-

{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about 5. The claims of US '896 are drawn to a pharmaceutical composition comprising a pharmaceutical propellant and crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1; further characterized by having five or more additional diffraction peaks at 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. Both sets of claims recite compositions comprising the same compound, in the same crystalline form. Instant claims 42-43 recite the composition to comprise an aqueous pharmaceutical carrier; instant claim 48 recites the composition as isotonic; claim 55 recites the composition to be buffered with a citrate buffer; and instant claim 56 recites the amount of crystalline freebase compound in the composition to range from about 0.05 µg-10 mg/mL. Although the patented claims don't explicitly recite these limitations, it would have been prima facie obvious to have incorporated an isotonic aqueous carrier, a citrate buffer, and the crystalline freebase compound in an amount from about 0.05 µg-10 mg/mL in view of Axt. Axt teaches crystalline forms of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-

carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in pharmaceutical compositions for treating pulmonary disorders (title & abstract; p. 2, lines 10-14 and 20-24). Axt teaches a specific embodiment wherein the composition comprises an isotonic aqueous solution containing the crystalline form of the compound, wherein the composition has a pH between 4-6, and is buffered with a citrate buffer (p. 3, lines 3-9). Axt further teaches an embodiment wherein the amount of the crystalline form of the compound present in the composition is from about 0.05 µg-10 mg/mL (p. 16, lines 25-30). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have incorporated these limitations into a pharmaceutical composition comprising a crystalline freebase of the patented compound. Although the instant claims don't recite the composition to further comprise a propellant as recited by the claims of US '896, or an additional agent selected from a beta-2 adrenergic agonist, steroidal anti-inflammatory agent, or PDE4 inhibitor, it would have been prima facie obvious to have incorporated a propellant and these additional agents in the instantly claimed composition in consideration of Axt. Axt teaches crystalline forms of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in pharmaceutical compositions for treating pulmonary disorders (title & abstract; p. 2, lines 10-14 and 20-24). Axt additionally teaches incorporating a propellant gas in the compositions; propellant gases such as 1,1,1,2-tetrafluoroethane, the propellant recited by claim 13 of US '896; and 1,1,1,2,3,3,3-heptafluoro-n-propane, the propellant recited by claim 8 of US '896, are also taught (p. 17, line 31-p. 18, line 14). As such, it would have been prima facie obvious to have further incorporated a propellant into the instantly claimed compositions, in consideration of Axt. Axt further teaches additional therapeutic agents can be incorporated into the

compositions, with beta-2 adrenergic agonists, steroidal anti-inflammatory agents, and phosphodiesterase-4 inhibitors explicitly taught as additional therapeutics for combination (p. 21, lines 7-13). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have incorporated these additional active agents in the instantly claimed compositions, in view of Axt. Claim 10 of US '896 further recites the compositions to comprise a surfactant selected from sorbitan trioleate, oleic acid, lecithin, and glycerin; although the instant claims don't explicitly recite these surfactants, Axt teaches the compositions to further comprise surfactants such as sorbitan trioleate, oleic acid, lecithin, and glycerin (p. 18, lines 9-11). The instant and patented claims are therefore obvious variants of each other in view of Axt, and are not patentably distinct.

6. Claims 41-43, 48-50, 53, and 55-68 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-3, 5-9, and 11-12 of U.S. Patent No. 9415041 B2 in view of Axt et. al., WO 2006099165 A1, cited in an IDS. The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about 5. The claims of US '041 are drawn to a pharmaceutical composition comprising a pharmaceutical dry powder excipient and crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester

characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1; further characterized by having five or more additional diffraction peaks at 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. Both sets of claims recite compositions comprising the same compound, in the same crystalline form. Instant claims 42-43 recite the composition to comprise an aqueous pharmaceutical carrier; instant claim 48 recites the composition as isotonic; claim 55 recites the composition to be buffered with a citrate buffer; and instant claim 56 recites the amount of crystalline freebase compound in the composition to range from about 0.05 µg-10 mg/mL. Although the patented claims don't explicitly recite these limitations, it would have been prima facie obvious to have incorporated an isotonic aqueous carrier, a citrate buffer, and the crystalline freebase compound in an amount from about 0.05 µg-10 mg/mL in view of Axt. Axt teaches crystalline forms of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in pharmaceutical compositions for treating pulmonary disorders (title & abstract; p. 2, lines 10-14 and 20-24). Axt teaches a specific embodiment wherein the composition comprises an isotonic aqueous solution containing the crystalline form of the compound, wherein the composition has a pH between 4-6, and is buffered with a citrate buffer (p. 3, lines 3-9). Axt further teaches an embodiment wherein the amount of the crystalline form of the compound present in the

composition is from about 0.05 µg-10 mg/mL (p. 16, lines 25-30). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have incorporated these limitations into a pharmaceutical composition comprising a crystalline freebase of the patented compound. Although the instant claims don't recite the composition to further comprise a dry powder excipient as recited by the claims of US '041, it would have been prima facie obvious to have incorporated a dry powder excipient in the instantly claimed composition in consideration of Axt. Axt teaches crystalline forms of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in pharmaceutical compositions for treating pulmonary disorders (title & abstract; p. 2, lines 10-14 and 20-24). Axt additionally teaches incorporating an excipient such as lactose or starch (p. 17, lines 2-6). As such, it would have been prima facie obvious to have further incorporated an excipient such as lactose or starch into the instantly claimed compositions, in consideration of Axt. Claim 2 of US '041 further recites the compositions to comprise an additional agent agent selected from beta-2 adrenergic agonists, steroidal anti-inflammatory agents, and phosphodiesterase-4 inhibitors; although the instant claims don't explicitly recite the compositions to further comprise one of these agents, Axt further teaches additional therapeutic agents can be incorporated into the compositions, with beta-2 adrenergic agonists, steroidal anti-inflammatory agents, and phosphodiesterase-4 inhibitors explicitly taught as additional therapeutics for combination (p. 21, lines 7-13). Formoterol is taught by Axt as a beta-2 adrenergic agonist (p. 21, lines 25-29). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have incorporated these additional active agents in the instantly claimed compositions, in view of

Axt. The instant and patented claims are therefore obvious variants of each other in view of Axt, and are not patentably distinct.

7. Claims 41-43, 48-50, 53, and 55-68 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 9765028 B2 in view of Axt et. al., WO 2006099165 A1, cited in an IDS. The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about 5. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. The claims of US '028 are drawn to crystalline freebase form III of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1; further characterized by five or more additional diffraction peaks at 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1; and a pharmaceutical composition comprising the same crystalline form and a pharmaceutically acceptable carrier. Instant claims

42-43 recite the composition to comprise an aqueous pharmaceutical carrier; instant claim 48 recites the composition as isotonic; claim 55 recites the composition to be buffered with a citrate buffer; and instant claim 56 recites the amount of crystalline freebase compound in the composition to range from about 0.05 µg-10 mg/mL. Although the patented claims don't explicitly recite these limitations, it would have been prima facie obvious to have incorporated an isotonic aqueous carrier, a citrate buffer, and the crystalline freebase compound in an amount from about 0.05 µg-10 mg/mL in view of Axt. Axt teaches crystalline forms of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in pharmaceutical compositions for treating pulmonary disorders (title & abstract; p. 2, lines 10-14 and 20-24). Axt teaches a specific embodiment wherein the composition comprises an isotonic aqueous solution containing the crystalline form of the compound, wherein the composition has a pH between 4-6, and is buffered with a citrate buffer (p. 3, lines 3-9). Axt further teaches an embodiment wherein the amount of the crystalline form of the compound present in the composition is from about 0.05 µg-10 mg/mL (p. 16, lines 25-30). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have incorporated these limitations into a pharmaceutical composition comprising a crystalline freebase of the patented compound. The instant and patented claims are not patentably distinct from each other.

8. Claims 41-43, 48-50, 53, and 55-68 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 10100013 B2. The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about 5. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. The claims of US '013 are drawn to a method for preparing a pharmaceutical composition comprising dissolving a crystalline freebase form III of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1; further characterized by five or more additional diffraction peaks at 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1, in a pharmaceutically acceptable aqueous carrier. Both sets of claims recite an aqueous solution that is also isotonic (patented claims 1 & 6, instant claims 42-43 & 53); buffered with a citrate buffer and having a pH of 4-6 (patented claims 7-8 & instant claim 55); and wherein the amount of crystalline freebase compound in the composition is from 0.05 µg-10 mg/mL (patented claim 9 & instant claim 56). The instant and patented claims are not patentably distinct from each

other, since both sets of claims require the same compound in the same crystalline form, in similar compositions.

9. Claims 41-43, 48-50, 53, and 55-68 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 10550081 B2 in view of Axt et. al., WO 2006099165 A1, cited in an IDS. The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about 5. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. The claims of US '081 are drawn to crystalline freebase form III of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a melting point of about 125°C; and having a DSC thermogram in accordance with Fig. 4. Instant claim 49 recites the crystalline form to have the same melting point of about 125°C; additionally, the disclosure recites this crystalline form to have a DSC thermogram that is identical to that of Fig. 4 as claimed in US '081 (see Fig. 4 of instant application, as well as p. 4 of the instant specification, lines 21-23). Instant claims 42-43 recite the composition to comprise an aqueous pharmaceutical carrier; instant claim 48 recites

the composition as isotonic; claim 55 recites the composition to be buffered with a citrate buffer; and instant claim 56 recites the amount of crystalline freebase compound in the composition to range from about 0.05 µg-10 mg/mL. Although the patented claims don't explicitly recite these limitations, it would have been prima facie obvious to have incorporated an isotonic aqueous carrier, a citrate buffer, and the crystalline freebase compound in an amount from about 0.05 µg-10 mg/mL in view of Axt. Axt teaches crystalline forms of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in pharmaceutical compositions for treating pulmonary disorders (title & abstract; p. 2, lines 10-14 and 20-24). Axt teaches a specific embodiment wherein the composition comprises an isotonic aqueous solution containing the crystalline form of the compound, wherein the composition has a pH between 4-6, and is buffered with a citrate buffer (p. 3, lines 3-9). Axt further teaches an embodiment wherein the amount of the crystalline form of the compound present in the composition is from about 0.05 µg-10 mg/mL (p. 16, lines 25-30). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have incorporated these limitations into a pharmaceutical composition comprising a crystalline freebase of the patented compound. The instant and patented claims are not patentably distinct from each other.

10. Claims 41-43, 48-50, 53, and 55-68 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 11008289 B2. The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-

ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about 5. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. The claims of US '289 are drawn to a method for treating COPD in a human patient comprising preparing a pharmaceutical composition by dissolving a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in an aqueous pharmaceutical carrier, wherein the crystalline freebase is characterized by diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1. Instant claim 49 and patented claim 4 recite the crystalline form to have the same melting point of about 125°C. Both sets of claims recite an aqueous pharmaceutical carrier (patented claim 1 & instant claims 42-43); an isotonic composition (patented claim 6 & instant claim 53); the composition to have a pH of about 5 (patented claims 7-8 & instant claim 41); and the composition to be buffered with a citrate buffer (patented claim 8 & instant claim 55). Instant claim 56 recites the composition to comprise the crystalline form in an amount of about 0.05 µg-10 mg/mL, and patented claim 9 recites the administered composition to comprise the same amount range of crystalline form. The instant and patented claims are not patentably distinct from each other, since both sets of claims require the same compound in the same crystalline form, in similar compositions.

11. Claims 41-43, 48-50, 53, 55-61, and 65-68 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 8921396 B2 in view of in view of Axt et. al., WO 2006099165 A1, cited in an IDS. The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about 5. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. The patented claims are drawn to methods of producing bronchodilation and treating COPD comprising administering to a patient by inhalation a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1; and having five or more additional diffraction peaks at 2θ values selected from 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. Instant claims 42-43 recite the composition to comprise an aqueous pharmaceutical carrier; instant claim 48 recites the composition as isotonic; claim 55 recites the composition to be buffered with a citrate buffer; and instant claim 56 recites the amount of crystalline freebase compound in the composition to range from about 0.05 µg-10 mg/mL. Although the patented

claims don't explicitly recite these limitations, it would have been prima facie obvious to have incorporated an isotonic aqueous carrier, a citrate buffer, and the crystalline freebase compound in an amount from about 0.05 µg-10 mg/mL in view of Axt. Axt teaches crystalline forms of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in pharmaceutical compositions for treating pulmonary disorders (title & abstract; p. 2, lines 10-14 and 20-24). Axt teaches a specific embodiment wherein the composition comprises an isotonic aqueous solution containing the crystalline form of the compound, wherein the composition has a pH between 4-6, and is buffered with a citrate buffer (p. 3, lines 3-9). Axt further teaches an embodiment wherein the amount of the crystalline form of the compound present in the composition is from about 0.05 µg-10 mg/mL (p. 16, lines 25-30). Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have incorporated these limitations into a pharmaceutical composition comprising a crystalline freebase of the patented compound. The instant and patented claims are not patentably distinct in consideration of Axt.

12. Claims 41-43, 48-50, 53, 55-61, and 65-68 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 21-41 of copending Application No. 17841567 (reference application). The instant claims are drawn to a pharmaceutical composition comprising crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, wherein the composition has a pH of about

5. Claim 48 of the instant application further recites the crystal form to have five or more additional diffraction peaks at: 8.8±0.1, 10.1±0.1, 11.4±0.1, 11.6±0.1, 14.8±0.1, 15.2±0.1, 16.1±0.1, 16.4±0.1, 16.9±0.1, 17.5±0.1, 18.2±0.1, 19.3±0.1, 19.9±0.1, 20.8±0.1, 21.1±0.1, 21.7±0.1, and 22.3±0.1. The copending claims are drawn to a process for preparing a pharmaceutical composition comprising dissolving a crystalline freebase of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}-ethyl)piperidin-4-yl ester in a solvent to form a solution, and a pharmaceutical composition comprising the same crystalline freebase compound; wherein the crystalline freebase is characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1. Claims 22-23 of appl. '567 further recite an aqueous pharmaceutical carrier as a solvent. Both sets of claims recite the crystalline form to have a melting point of about 125°C (instant claim 49, and copending claim 26); the composition to have a pH of about 5 (instant claim 41 and copending claim 30); wherein the composition is isotonic (instant claim 53 and copending claim 28); wherein the composition further comprises a citrate buffer (instant claim 55 & copending claim 30); and the composition to comprise the crystalline form in an amount of about 0.05 µg-10 mg/mL (instant claim 56 & copending claim 41). The instant and copending claims are not patentably distinct because they both encompass the same crystalline freebase form of the same compound.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Information Disclosure Statements

13. The IDS filed on 10/4/21 and 11/22/22 have been considered.

Conclusion

14. Claims 41-43, 48-50, 53, 55-68 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached Monday-Friday 9:00-5:30 EST.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kortney Klinkel can be reached on 571-270-5239. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SARAH . PIHONAK
Primary Examiner
Art Unit 1627

/SARAH PIHONAK/
Primary Examiner, Art Unit 1627

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183577 7590 04/12/2023

Sheppard Mullin Richter & Hampton LLP/Theravance
650 Town Center Drive, 10th Floor
Costa Mesa, CA 92626

EXAMINER
PIHONAK, SARAH

ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 04/12/2023

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/301,820	04/15/2021	Grahame Woollam	P-257-US9/71TD-343862-US9	1236

TITLE OF INVENTION: CRYSTALLINE FREEBASE FORMS OF A BIPHENYL COMPOUND

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	07/12/2023

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

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183577 7590 04/12/2023
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(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/301,820	04/15/2021	Grahame Woollam	P-257-US9/71TD-343862-US9	1236

TITLE OF INVENTION: CRYSTALLINE FREEBASE FORMS OF A BIPHENYL COMPOUND

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	07/12/2023

EXAMINER	ART UNIT	CLASS-SUBCLASS
PIHONAK, SARAH	1627	514-316000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

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PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

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❑ Applicant certifying micro entity status. See 37 CFR 1.29

❑ Applicant asserting small entity status. See 37 CFR 1.27

❑ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/301,820	04/15/2021	Grahame Woollam	P-257-US9/71TD 343862 US9	1236

183577 7590 04/12/2023

Sheppard Mullin Richter & Hampton LLP/Theravance
650 Town Center Drive, 10th Floor
Costa Mesa, CA 92626

EXAMINER	
PIHONAK, SARAH	

ART UNIT	PAPER NUMBER
1627	

DATE MAILED: 04/12/2023

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 17/301,820	Applicant(s) Woollam, Grahame	
	Examiner SARAH PIHONAK	Art Unit 1627	AIA (FITF) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to 3/23/23.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are See Continuation Sheet . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☐ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/SARAH PIHONAK/
Primary Examiner, Art Unit 1627

Continuation of 3. The allowed claim(s) is/are: 41-43,48-50,53 and 55-68

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Status of Claims

1. Claims 41-43, 48-50, 53, and 55-68 are pending as of the response filed on 3/23/23. Claims 1-40, 44-47, 51-52, and 54 have been canceled.

The provisional statutory double patenting rejection over the claims of copending application 17841567 is withdrawn in consideration of claim amendments filed in the copending application.

The terminal disclaimer filed on 3/23/23 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 17841567, US 8541451, US 9226896, US 8415041, US 9765028, US 10100013, US 10550081, US 11008289, and US 8921396 has been reviewed and is accepted. The terminal disclaimer has been recorded. The nonstatutory double patenting rejections over the claims of 17841567, US 8541451, US 9226896, US 8415041, US 9765028, US 10100013, US 10550081, US 11008289, and US 8921396 are withdrawn in consideration of the terminal disclaimer.

2. Claims 41-43, 48-50, 53, and 55-68 are allowed.

Reasons for Allowance

3. The following is an examiner's statement of reasons for allowance: the claimed pharmaceutical composition comprising crystalline freebase form of biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}ethyl)piperidin-4-yl ester

having a powder X-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1, in accordance with that shown in Fig. 1 (form III as defined in Applicant's specification), having a melting point of about 125°C is not taught or suggested by the closest prior art. Axt, WO 2006099165, and Mammen, US 20050203133, both cited in an IDS, represent the most relevant prior art. Axt teaches crystalline polymorphs I and II of freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}ethyl)piperidin-4-yl ester; however, these polymorphs are prepared by different processes (different solvents) from the instantly claimed crystalline polymorph, are characterized by different PXRD patterns, and the polymorphs of Axt have melting peaks at about 102.7 °C and 98.6 °C. Mammen teaches crystalline freebase biphenyl-2-ylcarbamic acid 1-(2-{[4-(4-carbamoylpiperidin-1-ylmethyl)benzoyl]methylamino}ethyl)piperidin-4-yl ester, however, this crystalline form is taught to be prepared by a different process compared to the crystalline form of the instant claims, using different solvents (Mammen teaches a combination of H_2O:acetonitrile at a 1:1 ratio or a combination of acetonitrile: MTBE at a 1:2 ratio, while the instantly claimed form is prepared using only acetonitrile, toluene, or a combination of isopropyl acetate:water). Mammen also does not teach or suggest the crystalline form having a powder X-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.6±0.1, 13.1±0.1, 18.6±0.1, 19.7±0.1, and 20.2±0.1.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the

issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Information Disclosure Statement

4. The IDS filed on 3/23/23 has been considered.

Conclusion

5. Claims 41-43, 48-50, 53, and 55-68 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached Monday-Friday 9:00-5:30 EST.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kortney Klinkel can be reached on 571-270-5239. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit:

https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SARAH . PIHONAK
Primary Examiner
Art Unit 1627

/SARAH PIHONAK/
Primary Examiner, Art Unit 1627